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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/813,506 | 03/29/2004 | Daniel D. Shoemaker | 9301-235-999 | 5273 |
| 20583 | 7590 | 11/14/2006 | EXAMINER | |
| JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017 | | | STAPLES, MARK | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1637 | |

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/813,506 | SHOEMAKER ET AL. | |
| | Examiner | Art Unit | |
| | Mark Staples | 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 10/16/2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 112 and 185-232 is/are pending in the application.
- 4a) Of the above claim(s) 178, 186-188, 190, 191, 193-196, 198, 199, 201-219, 225, and 227 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 112, 185, 189, 192, 197, 200, 220-224, 226, and 228-232 is/are rejected.
- 7) Claim(s) 228-231 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 03/29/2004 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>10/16/2006</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I claims 122, and 185-232 in the reply filed on September 14, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant elected the following species within Group I without traverse:

(1d) Array range is greater than 50,000 polynucleotides per cm² (claim 189 in part),

(2c) Genomic sequences for each probe is set apart from other probes by less than 200 bp (claim 192 in part),

(3b iii) nucleotide sequences of probes are 10-200 nucleotides (claim 197 in part) and genomic sequences for each probe is set apart from other probes by less than 200 bp (claim 200 in part), and

(4b) First plurality of probes is at least 10,000 probes (claim 226 in part).

Claims 189, 192, 197, 200, and 226 are directed to the elected species. Claims 186-188, 190, 191, 193-196, 198, 199, 201-219, 225, and 227 are directed to non-elected species. This clarification is made in response to Applicant's remarks concerning what are claims read on the elected species.

Claims 178 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention (Group II), there being no allowable generic or

linking claim. Election was made without traverse in the reply filed on September 14, 2006.

Claims 186-188, 190, 191, 193-196, 198, 199, 201-219, 225, and 227 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species in Group I, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on September 14, 2006.

In summary and as filed on 12 December 2001, claims 122, 185, 220-224, and 228-232 of Group I and claims 189, 192, 197, 200, and 226 of Group I consonant with the election of species will be fully examined for patentability.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should reflect that the invention is a product which is a positionally-addressable ordered array of

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polynucleotides. It is also noted that the claims of the instant application do not recite gene discovery as found in the current title.

4. The abstract of the disclosure is objected to because it refers to methods and systems. The claims of the instant application recite array products and do not recite methods and systems. Correction is required. See MPEP § 608.01(b).

5. The disclosure is objected to because of the following: The sequence submitted on paper and in Computer Readable Form (CRF) should be referenced within the specification by SEQ ID NO: 1. Appropriate correction is required.

6. The use of the trademark CY DYE™ has been noted in this application. It and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claims 228-231 are objected to because of the following informalities: confusing grammar in the construction: "further comprising a sample comprising a population of cellular or nucleic acid derived therefrom on the surface of said solid support". The construction of this phrase is confusing. It is confusing as to whether the entire sample is on the surface, or if just the population is on the surface, both of these are on the surface, or some other meaning is intended.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 122, 185, 189, 192, 197, 200, 220-224, 226, and 228-232 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 122 is indefinite since the claim recites "probes . . . comprising a sequence complementary . . . to a different genomic sequence" in lines 5 and 6 and later recites "respective genomic sequences for the probes". Probes with sequences complementary to genomic sequences need not be genomic sequences, as is the case for organisms having a single stranded genomic sequence. The complement to a single stranded genomic sequence is not a genomic sequence.

Claims 192 and 200 are indefinite since the claims recite "genomic sequences for each probe" which is in conflict with the base claim 122 recitation that the probes have sequences complementary to genomic sequences. This claim language alternatively may be intended to mean "genomic sequences targeted by each probe". The current claim language of claims 192 and 200 is indefinite.

Claims 122, 185, 189, 192, 197, 200, 221-224, 226, and 228-232 are indefinite because of the term "first plurality" in line 3 of claim 12, in line 1 of claim 226, and in line

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1 of claim 227. It is unclear what is meant by this term as only one plurality is recited in the claims; there is no "second plurality" or other plurality recited.

Claims 185, 189, 192, 197, 200, 221-224, 226, and 228-232 are indefinite because of the limitation "repetitive elements, simple repeats, or polyX repeats have been excluded" in lines 1 and 2 of claim 185 and in lines 2 and 3 of claim 232. It is unclear what number of repeats is to be excluded. No useable definitions of these terms was found in the specification. Rather these terms were explained by example and by what was preferable. As the specification discloses, repetitive elements can be just two repeated nucleotides. It is unclear if the limitation in the claims is intended to exclude all repetitive elements or perhaps repetitions above a certain number. Any clarification of this limitation should be supported by and referenced to the specification.

Claim 197 is indefinite because of the phrase "probes consist of in the range of 10-200 nucleotides". It is unclear how many nucleotides are in these probes. The following may be intended: "probes consist of 10-200 nucleotides".

Claim 220 is indefinite because it depends from a cancelled claim, claim 156.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 185, 189, 192, 197, 200, 221-224, 226, 228-232 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for arrays comprising polynucleotide probes, does not reasonably provide enablement for arrays

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comprising polynucleotide probes wherein repetitive elements, simple repeats, or polyX have been excluded. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 185, 189, 192, 197, 200, 221-224, 226, 228-232 recite the exclusion of any repetitive elements, simple repeats, or polyX repeats from probes (claim 185 and dependent claims and claim 232), which broadly claim exclusion of two or more nucleotide repeats from probes. The inventor does not provide an example where all two nucleotide repeats are excluded. No direction is provided on how to exclude two or even three-nucleotide repeats. As repeats of two or more nucleotides are frequent in nucleotide sequences (see for example SEQ ID NO: 1 of the instant application), one of ordinary skill in the art would not know how to exclude every repeat in order to make the claimed invention. The state of the prior art is such that much experimentation would be needed to make the invention, if in fact, it were possible to do so for the broadly claimed exclusion of two or more nucleotide repeats. Thus, the claimed invention is not enabled for exclusion of repetitive elements, simple repeats, or polyX repeats from probes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a)

11. Claim 220 is not examined in regards to prior art as it depends from a cancelled claim.

Due to the rejections on claims 122, 189, 192, 197, 200, 119-224, 226, and 228-231 in prior sections, these claims have been reasonably interpreted for examination in regards to prior art, as follows.

12. Claims 122, 189, 192, 197, 200, 119-222, 224, 226, and 228-231 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (US Patent No. 6,329,140 filed 1997), cited on the Information Disclosure Statement (IDS) and Bowtell (1999).

Regarding claim 122, Lockhart et al. teach an array, comprising:

a positionally-addressable ordered array of polynucleotide probe s bound to a solid support (entire reference especially Figures 1-4 and column 23 line 28-29: "Probes may be laid out on an polynucleotide array with a specifically defined positional relationship");

and said polynucleotide probes comprising a plurality of at least 100 polynucleotide probes of different nucleotide sequences (entire reference especially Figures 1-4 and claim 1 "at least four hundred different polynucleotides sequences per square centimeter"), each said different nucleotide sequence comprising a sequence complementary and hybridizable to a different genomic sequence of the same species of organism, said different genomic sequences being found at sequential sites in the genome of said species of organism (entire reference, especially Figure 2, Brief Description of the Figures, and SEQ ID NOS: 6-37 for the specie Homo Sapiens), wherein the distance between 5' ends of said sequential sites is always less than 500 bp (entire reference, especially "Single Increment Tiling" found in column 9 line 62 through column 10 line 7 in which each probe overlaps and where sequence signature includes nucleotide sequences at most 300, 250, 200, 150, 100, 75, 50, 30 , 25 or 15 nucleotides in length found in column 7 lines 36-38; and thus for overlapping sequences of 300 or less, the distance between 5' ends of any two sequential overlapping sites always must be less than 500 bp; as the maximum 5' distance end to end, which needs to include at least 1 overlapping nucleotide, is $300-1 = 299$ bp).

Regarding claim 189, Lockhart et al. an array with probe density ranging from 625 to 10 million probes per 1 cm² and thus teach an array having greater than 50,000 different polynucleotide probes per 1 cm². (col. 7, lines 1-9).

Claim 192 is interpreted as reciting an array where the genomic sequences targeted by the probes are spaced apart by less than 200 bp. Lockhart et al. teach an array where the sequences targeted by the probes are spaced apart by less than 200 bp (entire reference, especially “*Single Increment Tiling*” found in column 9 line 62 through column 10 line 7 in which each probe overlaps and where sequence signature include nucleotide sequences at most 300, 250, 200, 150, 100, 75, 50, 30, 25 or 15 nucleotides in length found in column 7 lines 36-38; and thus for overlapping sequences of 200 or less, the distance between 5’ ends of any two sequential overlapping sites always must be less than 200 bp; as the maximum 5’ distance end to end, which needs to include at least 1 overlapping nucleotide, is 200-1 = 199 bp).

Claim 197 is interpreted as reciting an array wherein each nucleotide sequence in the array consists of 10-200 nucleotides. Regarding claim 197, Lockhart et al. teach an array wherein each nucleotide sequence of the array consist of 102-103 nucleotide sequences as given in SEQ ID NOS: 5-37 (See Figure 5 and 6, Sequence Listing, and description of Figures 5 and 6 found in column 6 lines 49-67).

Regarding claims 221, 222 and 224, Lockhart et al. teach wherein the organism is a human, *Homo Sapiens*, which is a mammal which is an eukaryote (see Sequence Listing for SEQ ID NOS: 5-27 where the organism is *Homo Sapiens*, Figure 5 and 6, Sequence Listing, and description of Figures 5 and 6 found in column 6 lines 49-67).

Regarding claim 226, Lockhart et al. teach an array with at least 10,000 probes by teaching high density arrays, with probe density ranging from 625 to 10 million probes per 1 cm². (Fig. 2; col. 6, lines 62-67; col. 7).

Claims 228-231 are interpreted as reciting an array in contact with a sample containing cellular RNA or nucleic acid under conditions conducive to hybridization of target sequences in the cellular RNA or nucleic acid to the array probes. Regarding claims 228 and 230, Lockhart et al. teach "The target polynucleotide whose sequence is to be determined can be isolated from a clone, a cDNA, genomic DNA, RNA, cultured cells, or a tissue sample"; and further teaches "If the target is mRNA, the sample is obtained from a tissue in which the mRNA is expressed" and "sufficient DNA is present in the tissue sample to dispense with the amplification step", in other words the total cellular DNA, which is nucleic acid, is used (see column 21 lines 8-37 and entire reference).

Regarding claim 229, Lockhart et al. teach "The target can be labeled at one or more nucleotides during or after amplification" (see column 21 lines 33-34).

Regarding claim 231, Lockhart et al. teach an array with at least 10,000 different probes by teaching high density arrays of different probes, with probe density ranging from 625 to 10 million probes per 1 cm². (Fig. 2; col. 6, lines 62-67; col. 7).

Regarding claim 1, Lockhart et al. do not specifically teach an array wherein the genomic target sequences for a plurality of probes span a genomic region of at least 25,000 bp.

Bowtell teaches microarrays having regions of 42,000 (42k) and 30,000 (30k) gene sets, each of which is over 25,000 bp and that the entire genome of *C. elegans* (entire reference, especially Table 3, 2nd column first two entries, p. 26 column 2 - 2nd paragraph, and supporting document, Human Genome Project, p. 3 chart showing 3 billion base for the human genome and 97 million bases for *C. elegans* genome).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Lockhart et al. by spanning genomes as suggested by Bowtell with a reasonable expectation of success. The motivation to do so is provided by Bowtell who teach the usefulness of array to span genomes and the teaching of Lockhart et al. that array can span gene families (see Figure 3 and its description in column 5 lines 27-33). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

13. Claim 223 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (US Patent No. 6,329,140 filed 1997) and Bowtell (1999) as applied to claims 122, 189, 192, 197, 200, 119-222, 224, 226, and 228-231 above, and further in view of Schena et al. (1996).

Lockhart et al. and Bowtell teach as noted above.

Lockhart et al. and Bowtell do not teach wherein the organism is a plant.

Schena et al. teach microarrays to measure expression of plant genes (see 2nd paragraph of p. 10614).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Lockhart et al. and Bowtell by targeting nucleotide sequences of plant genes as suggested by Schena et al. with a reasonable expectation of success. The motivation to do so is provided by Schena et al. who teach usefulness of microarrays in measuring plant genes and the teaching of Lockhart et al. and Bowtell who teach the usefulness of microarrays. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

14. No claim is allowed.
15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
Examiner
Art Unit 1637
November 8, 2006

M/S

Kenneth R. Horlick
KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

11/8/06